

### DETAILED OFFICE ACTION

The request filed on 09 May 2011 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 10/646,308 is acceptable, and a RCE has been established. An action on the RCE follows.

Applicant's amendment filed on 09 May 2011 is acknowledged and entered. Following the amendment, claims 48, 52 and 65-67 are canceled, and claims 46 and 49 are amended.

Currently, claims 46, 47, 49, 51 and 64 are pending and under consideration.

#### **Withdrawal of Objections and Rejections:**

All objections and rejections of claims 48, 52 and 65-67 are moot as the applicant has canceled the claims.

#### **Rejections Over Prior Art:**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 46, 47, 49, 51 and 64 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Waelti (US2004/0028687) and Yndestad et al. (Cardiovasc Res., 2002 Apr; 54(1):175-82, provided by applicants), and in view of Goodwin et al. (US5,674,704, provided by applicants), for the reasons of record set forth in the previous Office Actions mailed on 5/13/09, 2/17/10, and 11/9/10.

Applicants argument filed on 09 May 2011 has been fully considered, but is not deemed persuasive for the reasons below.

At pages 4-5 of the response, applicants argue, citing case law, that rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention, and such an approach is impermissible under the current law; that the claimed invention must be viewed as a whole; and there is no teaching, suggestion or motivation in Yndestad, Goodwin or Waelti (or generally known in the art in 2003) to combine the prior art references to make the claimed invention, and that there is absolutely no information in Yndestad, Goodwin or Waelti suggesting a nexus between the 4-1BB pathway and chemotherapy-induced cardiotoxicity, and this is the inventive contribution of Applicants; and that one of skill in the art in August of 2003 would not connect this disparate art without the benefit of having read the present application. This argument is not persuasive for the following reasons: first, prior art searching would have to be based on what being claimed, and the present rejection is solely based on the teachings of the prior art, not on anything from the present disclosure. Further, in response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, the rejection was not made by randomly piecing together elements in the prior art, and the nexus was clearly indicated by the combined teachings of the prior art references. As addressed previously, Waelti teaches that one of the greatest limitations

of cancer chemotherapy agents such as are the severe side effects accompanying the use of some of the most broadly active antitumor agents, such as doxorubicin, which can cause dose-dependent cardiotoxicity often resulting in irreversible cardiomyopathy with serious congestive heart failure; Yudestad teaches that besides TNF $\alpha$  as a pathogenic factor in CHF, other members of the TNF superfamily including 4-1BB-L may potentially be even more important; and Goodwin teaches soluble 4-1BB polypeptides (SEQ ID NO:8 comprises amino acids 1-163 of the present SEQ ID NO:18 with 100% sequence identity), which retain the ability to bind the 4-1BB ligand, and fusion proteins thereof suitable for therapeutic applications. Therefore, it would be obvious to the person of ordinary skill in the art at the time the invention was made to target 4-1BB-L with Goodwin's soluble 4-1BB fusion protein for the treatment of cardiomyopathy/CHF including those caused by anthracycline compounds such as doxorubicin (taught by Waelti), as 4-1BB-L, which is a member of the TNF superfamily, is also overexpressed (besides TNF) in CHF patients (by Yudestad).

At page 5 of the response, applicants argue, citing case law, that that the only suggestion for the Examiner's combination of the isolated teachings of the applied references improperly stems from Applicants' disclosure, and it is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious, and that "Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). Applicants further argue that as the KSR Court stated "[R]ejections on obviousness grounds, cannot be sustained by mere conclusory statement; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." This argument is not persuasive for the reasons above. Further, the examiner has provided extensive and detailed explanations/reasoning/rational with support during the prosecution. Furthermore, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge

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gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

**Conclusion:**

No claim is allowed.

**Advisory Information:**

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dong Jiang/  
Primary Examiner, Art Unit 1646  
8/26/11